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(54) Process for the Preparation of
3,3-dimethyl-allyl Alcohol

(57) A 3,3-dimethyl-allyl halide is
reacted with an alkaline salt of a
carboxylic acid in an aqueous solution
and in the presence of a phase-

transfer catalyst to yield a 3,3-
dimethyl-allyl ester which is then
hydrolysed by treatment with an
aqueous solution of alkaline
hydroxide, in the presence of a phase-
transfer catalyst to yield 3,3-dimethyl-
allyl alcohol.

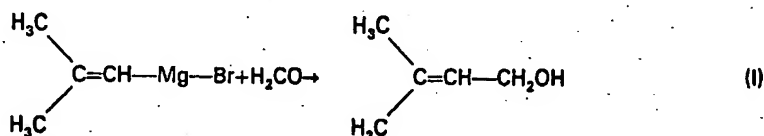
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SPECIFICATION

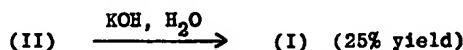
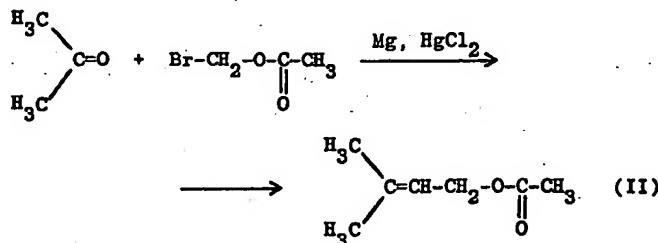
Process for the Preparation of 3,3-Dimethyl-allyl Alcohol

This invention relates to a process for the preparation of 3,3-dimethyl-allyl alcohol (3-methyl-but-2-en-1-ol) from 3,3-dimethyl-allyl halide.

There are various known methods for synthesizing 3,3-dimethyl-allyl alcohol. Some of these methods use organo-magnesium compounds (Grignard compounds), for example, the reaction between 2,2-dimethyl-vinyl-magnesium bromide and formaldehyde:



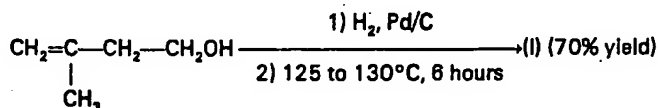
disclosed in H. Normant, Comptes Rendus Acad. Science (Paris), 240 314 (1955), and the reaction between acetone and 2-bromo-ethyl acetate in the presence of magnesium and mercuric chloride, followed by hydrolysis:



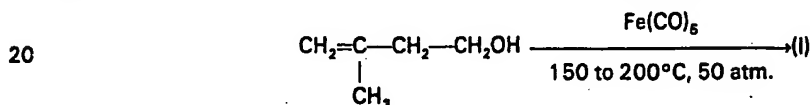
disclosed in R. F. Millar, F. F. Nord, Jour. of Org. Chem. 16, 728 (1951).

The above methods are not commercially viable since it is necessary to operate under anhydrous conditions and yields are low.

There are known synthesis methods that concern the isomerization of 2-methyl-buten-4-ol. For example the reaction:



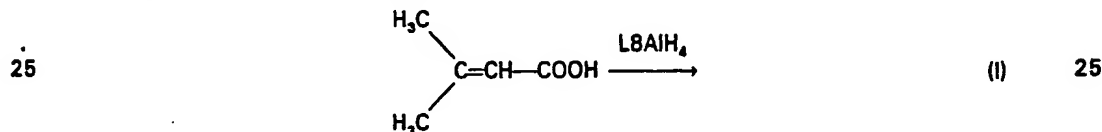
as disclosed in German Offenlegungsschrift No. 1,901,709 and the reaction:



as disclosed in French Patent Specification No. 1,594,968.

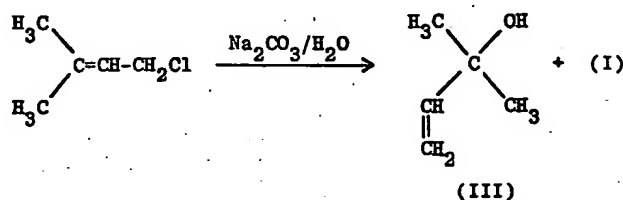
However these methods operate in the presence of inflammable and explosive gases and in the presence of toxic gas when carbon monoxide is present.

A synthesis method which is based on the reduction of β,β -dimethyl-acryl acid:

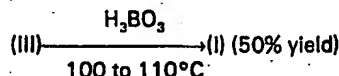


is disclosed in Jour. of Chem. Soc. (c) 811, (1971). However, lithium-aluminium hydride used as reducing agent, is well known to be a dangerous chemical.

Beilstein R. III 1 page 795 discloses that the direct hydrolysis of a 3,3-dimethyl-allyl halide with bases in an aqueous medium does not provide a good yield of 3,3-dimethyl-allyl alcohol, the main product consisting of an isomerization product, 3-methyl-buten-3-ol:



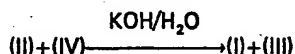
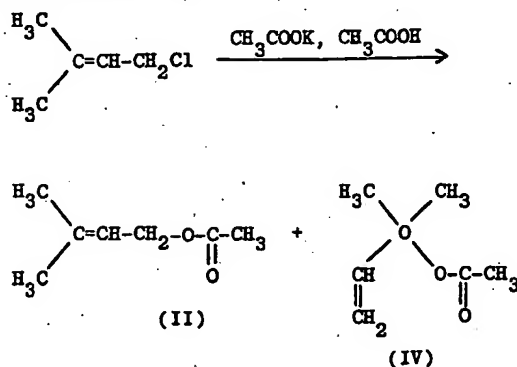
The tertiary alcohol (III) thus obtained may be converted to 3,3-dimethyl-allyl alcohol by treatment with boric acid:



5 as disclosed in I. N. Nazarov. S. S. Yufit, Zhur. Obs. Khim 29, 783 (1959) Chemical Abstract 54, 1280b. 5

A comprehensive process based upon the latter reactions would consist of a series of laborious passages consisting in the hydrolysis of the halide in the isomerization of compound (III) into (I) with boric acid. This would only lead to an enrichment of (I) in the mixture, the yield of such a reaction being 10 about 50%, followed by the separation by fractioned distillation of (I) from (III) and recycling of the latter. 10

A synthesis method which is based on the acetoxylation of the 3,3-dimethyl-allyl halide and the successive hydrolysis of the acetoxyated product:

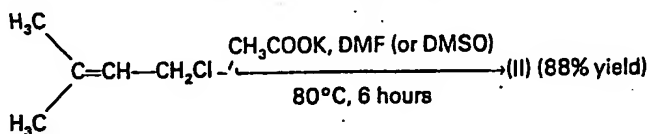


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is disclosed in I. N. Nazarov. I. N. Azerbaev, Zhur. Obs. Khim. 18, 407 (1968) — Chemical Abstract 43, 114 g (1969). However, the above acetoxylation is not free from isomerization reactions and about 30% of acetoxyated isomer (IV) is formed. When the mixture is then subjected to hydrolysis, further isomerization occurs and the tertiary alcohol (III) is the main product of the reaction.

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Japanese Patent Application No. J 52 095606, Nippon Zeon K. K. discloses a method for acetoxyating 3,3-dimethyl-allyl chloride, without the formation of unwanted isomerization products: 20



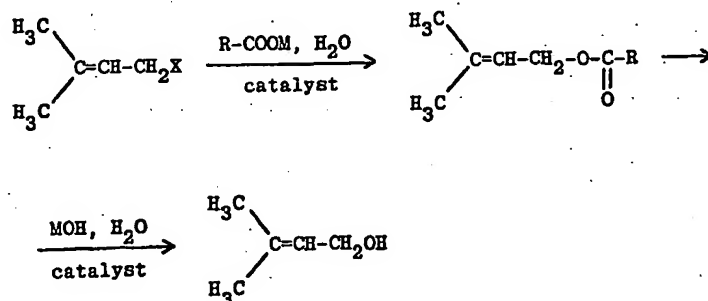
However, this method has the big drawback of using aprotic polar solvents which are very expensive and of difficult recovery of the product. Moreover, once the acetoxyated product (II) is obtained it is necessary to proceed to the hydrolysis, with the thereby involved drawbacks indicated above. 25

It is an object of the invention to provide an alternative process for the preparation of 3,3-dimethyl-allyl alcohol.

According to the invention there is provided a process for preparing 3,3-dimethyl-allyl alcohol in 30 which 3,3-dimethyl-allyl halide is reacted with an alkaline salt of a carboxylic acid in an aqueous solution and in the presence of a phase-transfer catalyst, to yield a 3,3-dimethyl-allyl ester which is then hydrolysed by treatment with an aqueous solution of alkaline hydroxide, in the presence of a phase-transfer catalyst to yield 3,3-dimethyl-allyl alcohol. 30

We have now found a process for the synthesis of 3,3-dimethyl-allyl alcohol, which consists of two successive stages. In the first stage, a 3,3-dimethyl-allyl halide, optionally dissolved in a water-immiscible solvent, e.g. an organic solvent, is reacted with an alkaline salt of a carboxylic acid in aqueous solution, in the presence of a phase-transfer catalyst, thereby obtaining the corresponding 3,3-dimethyl-allyl ester. In the second stage, the 3,3-dimethyl-allyl ester, optionally dissolved in a water-immiscible solvent, e.g. an organic solvent, is hydrolysed by treatment with an aqueous solution of an alkaline hydroxide in the presence of a phase-transfer catalyst.

A reaction scheme for a process of the invention may be represented schematically:



10 in which

X represents Cl or Br,
R represents H, alkyl, benzyl or aryl,
M represents Na or K, and
'catalyst' represents a phase-transfer catalyst.

15 The method of this invention provides 3,3-dimethyl-allyl alcohol with a high yield, without the formation of unwanted isomerization products. The method of the invention is particularly advantageous since it utilizes very cheap solvents, the reactants are safe and the process steps are simple to perform.

20 The first stage of the reaction utilizes a two phase system consisting of an organic and an aqueous phase in the presence of a phase-transfer catalyst. The organic phase consists of the 3,3-dimethyl-allyl halide, either alone or dissolved in an inert organic solvent immiscible with water, e.g. benzene, methylene chloride or petroleum ether. In general it is preferred to operate in the absence of the organic solvent, for reasons of practicability and economy. Excellent results are also obtained when using technical halide which contains isoprene.

25 The aqueous phase consists of an aqueous solution of an alkaline salt of a carboxylic acid, e.g. a propionate, a phenyl acetate or sodium or potassium benzoate, preferably sodium or potassium acetate. The amount of alkaline carboxylate used, is generally in a molar ratio of from 1 to 2 with respect to allyl halide.

30 In order to reduce the volume of the reaction mixture to a minimum it is preferred to use a saturated aqueous solution, optionally also in the presence of undissolved alkaline carboxylate at room temperature.

35 Suitable phase-transfer catalysts include a phosphonium salt, a crown-ether or, preferably, a quaternary ammonium salt which, in general, is economical. Ammonium salts supported on polymer substrates may also be used. Suitable quaternary ammonium salts include alkyl-ammonium halide (chloride or bromide), e.g. trimethylbenzylammonium chloride, tricaprilylmethylammonium chloride and tetrabutylammonium bromide. The quantity of quaternary ammonium salt used is generally from 0.1 to 10% based upon moles of the substrate. In order to control the initial exothermic activity of the reaction, it is preferable to utilize 0.5 to 1% of ammonium salt.

40 The reaction temperature is not critical and the reaction may be readily conducted from 0 to 80°C, although generally it is preferred to operate from room temperature to 50°C.

The duration of the reaction depends on the nature of the reactants, on the quantity of catalyst and on the reaction temperature. In general the reaction is completed within 1 to 3 hours.

The first stage of the process, according to a practical embodiment of the invention may be conducted in the following way.

45 A pre-established amount of alkaline carboxylate, an amount of water sufficient for dissolving the greatest part of the alkaline carboxylate and the phase-transfer catalyst are introduced into a reactor fitted with a stirrer and a thermometer at room temperature.

50 The reaction mixture is then subjected to stirring while 3,3-dimethyl-allyl halide, optionally dissolved in an organic solvent is slowly added. The temperature tends to rise spontaneously and is maintained at about 35°C using an external cooling bath of cold water. Once the admixing is accomplished and the exothermic action has stopped, the mixture is heated for 1 to 2 hours at 50 to 60°C in order to complete the reaction.

The organic phase is separated and treated with the usual laboratory techniques for separating the 3,3-dimethyl-allyl ester. It is not necessary to purify the ester which may be used as such.

The second stage of the process also involves the presence of an organic phase, an aqueous phase and a phase-transfer catalyst.

5 The organic phase consists of the 3,3-dimethyl-allyl ester obtained from the first stage optionally dissolved in an organic solvent immiscible with water, e.g. benzene, methylene chloride or petroleum ether. 5

The aqueous phase consists of an aqueous solution of an alkaline hydroxide, e.g. KOH or NaOH. The concentration of the aqueous alkaline hydroxide solution is not critical, however, it is preferred to use solutions having a concentration of about 50 to 60% by weight. In general an excess of alkaline hydroxide with respect to the ester is used. 10 10

The phase-transfer catalysts in the second stage may be any of the catalysts listed for the first stage and they may be used in the same quantities.

The reaction time depends on various factors, e.g. the nature of the reactants, the quantity of catalyst and the reaction temperature. In general, the reaction is completed over a period of 1 to 3 hours. 15 15

According to a practical form of embodiment, the second stage of the process is conducted in the following way.

A reactor provided with a stirrer and a thermometer is charged with the aqueous solution of alkaline hydroxide and the phase-transfer catalyst. The mixture is then vigorously stirred, during which time 3,3-dimethyl-allyl ester, optionally dissolved in an organic solvent is slowly added. 20 20

The initial exothermic reaction is controlled and the temperature is maintained at about 35°C using an external bath of cold water. Thereupon, the mixture is optionally heated for 1 to 2 hours at 50°C to complete the reaction. The organic phase is then separated and treated according to the conventional laboratory methods. The 3,3-dimethyl-allyl alcohol thus obtained, may be purified by distillation. 25 25

It is important to stress that under the experimental conditions described in the second stage, the direct hydrolysis of the 3,3-dimethyl-allyl halide does not take place, as will be illustrated in Example 3 hereinafter.

30 The process of this invention offers many advantages over the prior art. The main advantages may be summarised as follows: 30

the process provides 3,3-dimethyl-allyl alcohol in high yields,
the reaction product is free from by-products due to isomerization reactions,
the operating procedure is simple and no sophisticated equipment, such as a high pressure reactor, is required, no dangerous or highly expensive reactants, catalysts or solvents are used, 35 35
the starting product, for both stages, need not be particularly pure,
3,3-dimethyl-allyl halides of a technical quality, containing even up to 20% of isoprene may be used and it is not necessary to purify the 3,3-dimethyl-allyl ester obtained in the first stage.

The two stages of the process may be carried out independently from each other. The first stage may be exploited only for the preparation of 3,3-dimethyl-allyl esters without converting these latter to 3,3-dimethyl-allyl alcohol. Moreover, the second stage may be used separately for hydrolysing a 3,3-dimethyl-allyl ester of any origin, since it is not limited to the hydrolysis of 3,3-dimethyl-allyl esters prepared as described in the first stage. 40 40

It would appear from present knowledge of phase-transfer catalysed reactions that the process of the invention could be conducted according to other procedures, which are purely technological alternatives, for example the polyphasic systems generally comprised in the phase-transfer technique such as those reported in Chapter 1 of Phase Transfer Catalysts, Principles and Techniques of C. M. Starks and C. Liotta, Academic Press, New York, 1978. 45 45

3,3-Dimethyl-allyl alcohol finds various different uses in organic chemistry. The main uses relate to the synthesis of natural organic substances (terpenic derivatives), to the production of aromatizing substances and to the production of pesticides. For example, 3,3-dimethyl-allyl alcohol is the starting product for the synthesis of pesticides belonging to the class of pyrethroids, K. Kondo, K. Matsui, A. Negishi in "Synthetic Pyrethroids", T. Elliot Editor, ACS Symposium Series No. 42, pages 128 to 136. 50 50

The invention will now be illustrated by the following Examples.

55 Example 1 55

Preparation of 3,3-dimethyl-allyl-acetate (II)

A glass flask, fitted with a stirrer and a thermometer was charged with 2 moles of potassium acetate, 0.01 moles of tetrabutyl-ammonium chloride and 50 ml of water. The mixture was kept under constant stirring at room temperature and 1 mole of 3,3-dimethyl-allyl bromide (of technical degree, 60 60
containing about 20% by weight of isoprene) was slowly admixed over a period of 1 hour.

The reaction mixture heated up spontaneously during the addition and the temperature was maintained at about 35°C by means of an external bath of cold water. On completion of the addition the reaction mixture was kept under stirring at 60°C for 2 hours.

After cooling to room temperature, the reaction mixture was filtered in order to eliminate undissolved salts. The organic phase was then separated, washed with water until attaining a neutral pH, and finally was dried over anhydrous sodium sulphate.

130 g of a raw product which consisted for 92% (by gas-liquid-chromatograph GLC) of 3,3-dimethyl-allyl acetate (93% yield) were obtained which may be purified by distillation (boiling point=149 to 151°C). The I.R. and NMR spectra were consistent with the assigned structure. By GLC no peaks corresponding to isomerisation products were found.

Example 2

Preparation of 3,3-dimethyl-allyl Alcohol (I)

A mixture of 2 moles of potassium hydroxide at 85% concentration, 0.01 moles of tetrabutyl-ammonium bromide, and 50 ml of water was maintained under constant stirring at room temperature and 130 g of the raw product obtained in Example 1, containing about 92% of 3,3-dimethyl-allyl acetate were slowly added over a period of 1 hour. During the addition, the temperature rose spontaneously and was controlled by an external bath of cold water.

Once the admixture had been completed and the exothermic activity had subsided, the reaction mixture was stirred for 2 hours at 50°C. The reaction mixture was then cooled to room temperature, filtered, the organic phase was separated and washed with water until attaining a neutral pH, and thereafter it was dried over anhydrous sodium sulphate.

The 3,3-dimethyl-allyl alcohol was then purified by distillation (boiling point=140 to 142°C). 69 g of pure (I) were obtained with a purity of 96% determined by GLC. No peaks corresponding to isomerisation products were found.

The I.R. and NMR spectra were in accordance with the assigned structure. The total yield of the process was of about 80% with respect to the 3,3-dimethyl-allyl bromide.

Example 3

This Example illustrates that under the experimental conditions described in Example 2, no direct hydrolysis of the 3,3-dimethyl-allyl bromide occurs.

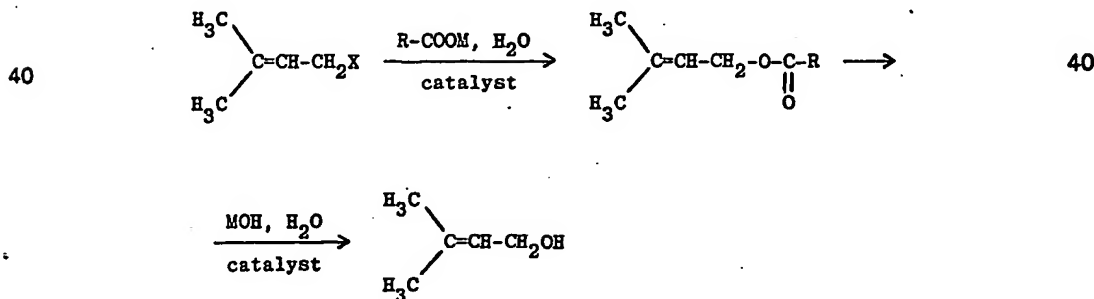
0.1 mole of technical 3,3-dimethyl-allyl bromide were added over a period of 5 minutes to an 85% potassium hydroxide solution (0.2 moles) in 5 ml of water, in the presence of 0.32 g of tetrabutyl-ammonium bromide. No exothermic action was observed.

The reaction mixture was kept under stirring for 1 hour, at room temperature. During this period samples were periodically drawn off which were then examined by I.R. spectroscopy. After 1 hour no reaction could be observed. The 3,3-dimethyl-allyl bromide was completely recovered.

Claims

1. A process for preparing 3,3-dimethyl-allyl alcohol in which 3,3-dimethyl-allyl halide is reacted with an alkaline salt of a carboxylic acid in an aqueous solution and in the presence of a phase-transfer catalyst, to yield a 3,3-dimethyl-allyl ester which is then hydrolysed by treatment with an aqueous solution of alkaline hydroxide in the presence of a phase-transfer catalyst to yield 3,3-dimethyl-allyl alcohol.

2. A process as claimed in Claim 1 conducted in accordance with the reaction scheme:



In which

X represents a chlorine or bromine atom,
R represents a hydrogen atom or an alkyl, benzyl or aryl group,
M represents sodium or potassium, and
'catalyst' represents a phase-transfer catalyst.

3. A process as claimed in Claim 1 or Claim 2 in which the phase-transfer catalyst comprises a cyclic polyether (crown ether), a phosphonium salt or, a quaternary ammonium salt optionally supported on polymers.

4. A process as claimed in Claim 3 in which the phase-transfer catalyst is a quaternary ammonium halide.

5. A process as claimed in Claim 4 in which the phase-transfer catalyst is tetra-butyl ammonium bromide.
6. A process as claimed in Claim 4 or Claim 5 in which the phase-transfer catalyst is present in an amount from 0.1 to 10 mole percent with respect to 3,3-dimethyl-allyl halide.
- 5 7. A process as claimed in any preceding claim in which the 3,3-dimethyl-allyl halide is dissolved in an inert solvent immiscible with water. 5
8. A process as claimed in Claim 7 in which the solvent is benzene, methylene chloride or petroleum ether.
9. A process as claimed in any one of Claims 1 to 6 in which the 3,3-dimethyl-allyl halide is used in the absence of organic solvents. 10 10
10. A process as claimed in any preceding claim in which the alkaline salt of the carboxylic acid is used in a molar ratio from 1 to 2 with respect to the 3,3-dimethyl-allyl halide.
11. A process as claimed in any preceding claim in which the alkaline salt of the carboxylic acid is sodium or potassium acetate.
- 15 12. A process as claimed in any preceding claim in which the aqueous solution of the alkaline salt of the carboxylic acid is a saturated solution. 15
13. A process as claimed in Claim 12 in which said saturated solution is in the presence of an undissolved salt.
14. A process as claimed in any preceding claim in which the reaction between 3,3-dimethyl-allyl halide and the alkaline salt of the carboxylic acid is carried out by slowly adding the halide to a concentrated solution of alkaline salt in the presence of a phase-transfer catalyst, maintaining the aqueous solution under vigorous stirring. 20 20
15. A process as claimed in any preceding claim in which the reaction between the 3,3-dimethyl-allyl halide and the alkaline salt of a carboxylic acid is conducted at a temperature from 0 to 80°C.
- 25 16. A process as claimed in Claim 15 in which said reaction is conducted at a temperature from room temperature to 60°C. 25
17. A process as claimed in any preceding claim in which the 3,3-dimethyl-allyl ester is reacted with the aqueous solution of an alkaline hydroxide, dissolved in an inert organic solvent immiscible with water.
- 30 18. A process as claimed in Claim 17 in which the inert organic solvent is benzene, methylene chloride or petroleum ether. 30
19. A process as claimed in any one of Claims 1 to 16 in which the 3,3-dimethyl-allyl ester is reacted with the aqueous solution of alkaline hydroxide as such in the absence of an organic solvent.
20. A process as claimed in any preceding claim in which the alkaline hydroxide is NaOH or KOH.
- 35 21. A process as claimed in any preceding claim in which the alkaline hydroxide is used in a molar ratio of from 1 to 2 with respect to the 3,3-dimethyl-allyl ester. 35
22. A process as claimed in any preceding claim in which the reaction between the 3,3-dimethyl-allyl ester and the aqueous solution of alkaline hydroxide is carried out by slowly adding the ester to the alkaline solution in the presence of a phase-transfer catalyst and maintaining the alkaline solution under vigorous solution. 40 40
23. A process as claimed in any preceding claim in which the reaction between 3,3-dimethyl-allyl ester and the alkaline solution is carried out at a temperature of from 0 to 60°C.
24. A process as claimed in Claim 23 in which said reaction is conducted at a temperature of from room temperature to 50°C.
- 45 25. A process for preparing 3,3-dimethyl-allyl alcohol in which a 3,3-dimethyl-allyl ester is hydrolysed by treatment with an aqueous solution of an alkaline hydroxide in the presence of a phase-transfer catalyst to yield 3,3-dimethyl-allyl alcohol. 45
26. A process for preparing 3,3-dimethyl-allyl alcohol substantially as herein described with reference to Example 2.